EXHIBIT 4

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THOMAS P. STEINDLER (*Pro Hac Vice*)
tsteindler@mwe.com
DAVID MLAVER (*Pro Hac Vice*)
dmlaver@mwe.com
MCDERMOTT WILL & EMERY LLP
500 N. Capitol St., N.W.
Washington, DC 20001
Tel: (202) 756-8000
Fax: (202) 756-8087

WILLIAM G. GAEDE III (SBN: 136184)
wgaede@mwe.com
MCDERMOTT WILL & EMERY LLP
275 Middlefield Road, Suite 100
Menlo Park, CA 94025
Tel: (650) 815-7400
Fax: (650) 469-1470

KATHERINE NICOLE CLOUSE (*Pro Hac Vice)*
nclouse@mwe.com
MCDERMOTT WILL & EMERY LLP
28 State Street
Boston, MA 02109
Tel: (617) 535-4000
Fax: (617) 535-3800

Attorneys for Defendant
Novartis Pharmaceuticals Corporation

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

OAKLAND DIVISION

PLEXXIKON INC.,

Plaintiff,

v.

NOVARTIS PHARMACEUTICALS CORPORATION,

Defendant.

CASE NO. 4:17-cv-04405-HSG (EDL)

DEFENDANT NOVARTIS PHARMACEUTICALS CORPORATION'S RESPONSIVE DAMAGES CONTENTIONS PURSUANT TO PATENT L.R. 3-9

drug is approved for a separate use apart from the treatment of metastatic melanoma that the other is not. Tafinlar® is approved for treatment of non-small cell lung cancer; Zelboraf® is not. Zelboraf® is approved for Erdheim-Chester Disease; Tafinlar® is not. Plexxikon's damages contentions ignore these facts. Assuming that competition between Zelboraf® and Tafinlar® were relevant to a damages analysis (which, as explained below, it is not), these factors must be taken into consideration.

The relevant market is also larger than just Tafinlar® and Zelboraf®. Even the submarket for "targeted" or "selective" BRAF inhibitors includes not only Tafinlar® and Zelboraf® but those products used in combination with Mekinist® and Cotellic®. Both Tafinlar® and Zelboraf® are sometimes prescribed as monotherapies for metastatic melanoma but more often are prescribed as combination therapies. In addition, there are other drugs that are not targeted therapies that are approved and used for the treatment of metastatic melanoma, including metastatic melanoma with BRAF V600E. The most important of these are a class of drugs known as "immunotherapies," which includes Opdivo® (Nivolumab) (Bristol-Myers Squibb), Yervoy® (ipilimumab) (Bristol-Myers Squibb), and Keytruda® (pembrolizumab) (Merck & Co.). Other relevant drugs may include Proleukin® (interleukin-2) and Sylatron® (peginterferon Alfa-2b), among others.[3] Plexxikon's attempt to portray Tafinlar® and Zelboraf® as competing in a two-product market is inaccurate.

Moreover, the therapeutic landscape for the drugs used to treat metastatic melanoma has changed rapidly over the course of the past decade. This timeline also cannot be ignored in a damages analysis. Some of the pertinent dates are as follows:

[3] The National Institutes of Health's National Cancer Institute lists 26 drugs approved for melanoma on its website. See https://www.cancer.gov/about-cancer/treatment/drugs/melanoma, last visited April 27, 2018.

- September 22, 2017 – Opdivo® is approved for patients with hepatocellular carcinoma who have previously been treated with sorafenib.
- September 22, 2017 – Keytruda® receives accelerated approval for gastric cancer.
- November 6, 2017 – Zelboraf® (alone, not in combination with Cotellic®) receives additional indication for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation.
- May 4, 2018 – Tafinlar® and Mekinist® are approved in combination for the treatment of unresectable or metastatic anaplastic thyroid cancer with BRAF V600E mutation.

Plexxikon ignores this history and the state of the market prior to the issuance of the patents-in-suit in its damages contentions, both in connection with its reasonable royalty analyses and in its lost royalties/price erosion theories.

II. REASONABLE ROYALTY

Two categories of compensation for infringement are the patentee's lost profits and a reasonable royalty. In this case, Novartis contends that the only form of damages available to Plexxikon would be a reasonable royalty, because Plexxikon itself does not sell any products. *See*, *e.g.*, *Warsaw Orthopedic, Inc. v. Nuvasive, Inc.*, 778 F.3d 1365 (Fed. Cir. 2015) ("To be entitled to lost profits, we have long recognized that the lost profits must come from the lost sales of a product or service the patentee itself was selling"); *Spine Solutions, Inc. v. Medtronic Sofamor Danek USA, Inc.*, 620 F.3d 1305, 1309 (Fed. Cir. 2010) ("It is undisputed that SSI [the patentee] does not sell any products. Therefore, [the patentee] is not entitled to any lost profits damages."); *Poly-America, L.P. v. GSE Lining Tech., Inc.*, 383 F.3d 1303, 1311 (Fed. Cir. 2004) ("A patentee needs to be selling some item, the profits of which have been lost due to infringing sales, in order to claim damages consisting of lost profits.").

Indeed, discovery may show that, on balance, it is Zelboraf® that is free riding on Tafinlar®, rather than the other way around, and that the introduction of Tafinlar® engendered expansion in the targeted therapy sub-market that has inured to the benefit of Zelboraf®. Put another way, it may turn out that Tafinlar® sales have grown the overall submarket for targeted therapies, and that Zelboraf® sales are higher than they would otherwise have been if Tafinlar® had not entered the market.

Plexxikon also contends that because [redacted] Once again, the hypothetical negotiation in this case does not involve "allowing a second competitor into the market." The second competitor (Tafinlar®) had *already been in the market* for more than three years prior to the date of the hypothetical negotiation, and would remain in the market following the hypothetical negotiation. The question is what would be a reasonable royalty to be paid for sales of Tafinlar® after the issuance of the patents-in-suit through the date of a final judgment in this case.

Plexxikon further contends that the amount Novartis paid GSK to acquire Tafinlar® "underscores the losses that Zelboraf® would be expected to take as a result of Novartis selling a competitive product." Plexxikon Damages Contention at 6. That argument is conceptually misguided as a matter of law. A reasonable royalty "compensates the owner *not for the damage he suffered*, but for the value of what was taken." *Warsaw Orthopedic, Inc.*, 778 F.3d at 1376 (emphasis added). Here, as noted above, the incremental value of the patents-in-suit over the prior art is negligible. Plexxikon further argues that the amount Novartis paid in 2015 for Tafinlar® shows it would have been willing to pay a "significant royalty" to get a license to the patents-in-suit in the hypothetical negotiation. But the patents-in-suit would have had zero value to Novartis other than for freedom to operate.

negatively affected those companies' sales, which in turn negatively affected the royalty payments made to plaintiffs. *Id.* at 1376. The Federal Circuit held that the lost royalty payments were not recoverable, stating that '[t]o be entitled to lost profits, we have long recognized that the lost profits must come from the lost sale of a product or service the patentee *itself* was selling." Id. (emphasis added). *See also Spine Solutions, Inc. v. Medtronic Sofamor Danek USA, Inc.*, 620 F.3d 1305, 1319 (Fed. Cir. 2010) (patentee not entitled to lost profits damages because it did not sell any products); *Poly-America, L.P. v. GSE Lining Tech., Inc.*, 383 F.3d 1303, 1311 (Fed. Cir. 2004) (same). Accordingly, Novartis contends that Plexxikon is not entitled to recover lost royalties as a matter of law.

Even assuming, *arguendo*, that Plexxikon is entitled to recover lost royalties (which it is not), Novartis contends that Plexxikon cannot establish it has lost royalties as a result of Tafinlar® sales.

At the outset, Plexxikon asserts that "Tafinlar® and Zelboraf® are the only two drugs in the relevant market – namely the market for selective BRAF inhibitors." This is wrong in several critical respects. First, as discussed above, the market for selective BRAF inhibitors is not the relevant market. There are other products, including the immunotherapies, which also compete in the same market. Second, Tafinlar® and Zelboraf® are each approved for at least one indication that the other is not. Moreover, combination use with Cotellic® and Mekinist® plays a role as well. In short, Novartis contends that given the presence of multiple non-infringing substitutes in a highly complex and dynamic market with multiple indications, Plexxikon will not be able to prove that Roche would have made any additional sales of Zelboraf® "but for" the alleged infringement by Novartis under the four-factor test set out in *Panduit Corp. v. Stahlin Bros. Fibre Works*, 575 F.2d 1552 (6th Cir. 1978). Novartis is not able to respond further to Plexxikon's lost royalties theory given the preliminary nature of Plexxikon's contentions.

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Respectfully submitted,

/s/ Thomas P. Steindler

THOMAS P. STEINDLER (*Pro Hac Vice*)
tsteindler@mwe.com
DAVID MLAVER (*Pro Hac Vice*)
dmlaver@mwe.com
MCDERMOTT WILL & EMERY LLP
500 N. Capitol St., N.W.
Washington, DC 20001
Tel: (202) 756-8000
Fax: (202) 756-8087

WILLIAM G. GAEDE III (SBN: 136184)
wgaede@mwe.com
McDermott Will & Emery LLP
275 Middlefield Road, Suite 100
Menlo Park, CA 94025
Tel: (650) 815-7400
Fax: (650) 469-1470

KATHERINE NICOLE CLOUSE (Pro Hac Vice)
nclouse@mwe.com
McDermott Will & Emery LLP
28 State Street
Boston, MA 02109
Tel: (617) 535-4000
Fax: (617) 535-3800

Attorneys for Defendant
Novartis Pharmaceuticals Corporation

CERTIFICATE OF SERVICE

The undersigned attorney hereby certifies that on May 9, 2018, the foregoing was served on counsel for Plaintiff Plexxikon Inc. by electronic mail to at least the following addresses:

- SERVICE-BRAF@durietangri.com and
- Plexxikon@youngbasile.com

By: /s/ *David Mlaver*
David Mlaver (*Pro Hac Vice*)

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